



## Occupational asthma, rhinitis, and contact urticaria caused by oxidative hair dyes in hairdressers

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### ARTICLE INFO

#### Article history:

Received for publication May 21, 2013.

Received in revised form August 29, 2013.

Accepted for publication October 3, 2013.

### ABSTRACT

**Background:** Oxidative hair dyes commonly contain paraphenylenediamine (PPD) and its derivatives, a well-known cause of delayed hypersensitivity among both consumers and hairdressers. They are also considered possible causes of occupational respiratory diseases. Despite the widespread use of hair dyes, there are only a few reports of asthma, rhinitis, and contact urticaria caused by PPD and related compounds. **Objective:** To characterize patients with occupational asthma, rhinitis, or contact urticaria associated with oxidative hair dyes and to evaluate the diagnostic methods.

**Methods:** We reviewed the patient files of the Finnish Institute of Occupational Health for the period January 1, 2001, through May 31, 2011, to identify patients diagnosed as having asthma, rhinitis, or contact urticaria associated with oxidative hair dyes. The diagnoses of asthma and rhinitis were based on specific inhalation challenges with hair dye products. Skin prick tests were performed with hair dye ingredients as hapten conjugates of human serum albumin and with hair dye products and ingredients as is. Open skin tests confirmed the diagnosis of contact urticaria.

**Results:** We describe 11 hairdressers with occupational asthma (5 cases), rhinitis (5 cases), and contact urticaria (3 cases) due to hair dyes. Of the 52 specific inhalation challenges performed, 9 (17%) had positive results. One patient who experienced an anaphylactic reaction when having her own hair dyed had positive skin prick test results to PPD and toluene-2,5-diamine sulfate.

**Conclusion:** Hairdressers are at risk for occupational asthma, rhinitis, and contact urticaria due to oxidative hair dyes. Skin prick testing may be insensitive for detecting immediate hypersensitivity to PPD and related compounds.

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### Introduction

Respiratory symptoms and contact dermatitis are frequent concerns among hairdressers.<sup>1–3</sup> Hairdressers are at an increased risk of occupational hand eczema due to frequent contact with the skin irritants and contact allergens in hairdressing chemicals.<sup>4</sup> They are also exposed to several airborne irritating factors<sup>5,6</sup> and allergens in their work, such as the persulfate salts in hair bleaching products, which are a major known cause of occupational asthma (OA) and occupational rhinitis (OR) among hairdressers.<sup>7–12</sup>

Paraphenylenediamine (PPD), an organic aromatic amine, is a common ingredient of oxidative hair dyes.<sup>13</sup> PPD and its derivatives are known as potent skin sensitizers,<sup>14</sup> and positive patch test reactions to PPD are frequent among patients with dermatitis.<sup>15–17</sup> The predominant cause of delayed contact allergy to PPD is exposure

to oxidative hair dyes.<sup>18</sup> Delayed contact allergy to PPD and related para-amino compounds, such as toluene-2,5-diamine sulfate (TDS), are a well-known cause of allergic contact dermatitis in both hairdressers and consumers who dye their hair.<sup>19</sup> Hairdressers and beauticians are at an increased risk of delayed PPD sensitization,<sup>20</sup> and the reported prevalences of PPD sensitization among hairdressers with dermatitis have been high (24% to 54%).<sup>21,22</sup> Several studies have reported an increasing frequency of delayed PPD sensitization,<sup>16,23</sup> most probably resulting from the increased use of hair dyes.<sup>24</sup>

Previously, only a few cases of immediate hypersensitivity to PPD have been reported in the literature.<sup>25–28</sup> Anaphylaxis associated with exposure to hair dyes that contain PPD or related compounds may occur,<sup>29–31</sup> and even one fatal case of anaphylaxis from hair dye use has been reported.<sup>32</sup> Airborne exposure to PPD has been associated with respiratory symptoms.<sup>33,34</sup> However, few previous reports exist on OA and OR due to PPD.<sup>9,35,36</sup>

The aim of the present study was to characterize patient cases of occupational immediate-type skin and respiratory diseases

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**Disclosures:** Authors have nothing to disclose.

associated with oxidative hair dye exposure. We describe 11 cases of hairdressers diagnosed as having immediate-type reactions (ie, OA, OR, and occupational contact urticaria [OCU]) caused by hair dyes containing PPD-related para-amino compounds and the diagnostic methods used. One of the patients experienced an anaphylactic reaction when having her own hair dyed with an oxidative hair dye that contained TDS.

## Methods

### Study Participants

The occupational medicine clinic at the Finnish Institute of Occupational Health receives patients with suspected occupational disease from all over Finland, which has a population of approximately 5.4 million. Work-related respiratory and dermatologic symptoms are the most common indications for referral to the clinic. The routine examinations of hairdressers referred to the clinic for immediate-type work-related symptoms include skin prick tests (SPTs) with common environmental allergens and the most common hairdressing chemicals. In case of respiratory symptoms, lung function tests (spirometry and histamine challenge) and exhaled nitric oxide measurement are performed, and serial peak flow monitoring at work and off work is included whenever feasible. Specific challenge tests (inhalation and skin) are used to confirm the diagnosis. We retrospectively reviewed the medical files of patients with a suspected occupational disease for the period of January 1, 2001, through May 31, 2011, to identify patients diagnosed as having OCU, OR, or OA associated with oxidative hair dyes. We also reviewed the files for SPTs and specific inhalation challenges (SICs) performed with oxidative hair dyes at the clinic during the same period. From the medical records, we collected data on the patients' occupational history, exposure to hair dye products, type of symptoms related to work (cutaneous, bronchial, and nasal), the association between symptoms and specific substances or work tasks, the duration of exposure before the onset of symptoms, the duration of symptoms before diagnosis, and the history of atopy and smoking. We also examined the results of the clinical examinations, immunologic tests, and SICs.

### SPTs and Measurement of Serum IgE

SPTs with common environmental allergens were performed with standardized allergen extracts of birch, alder, timothy grass, meadow fescue, mugwort, cat, dog, horse, cow, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Alternaria alternata*, *Cladosporium herbarum* (ALK, Copenhagen, Denmark), and natural rubber latex (Stallergenes SA, Antony, France). These tests included histamine hydrochloride (10 mg/mL) and a diluent control.

SPTs with PPD and TDS were performed with hapten conjugates of human serum albumin (HSA) prepared according to the method of Howe et al.<sup>37</sup> Three of the patients also underwent SPTs with hair dye products and hair dye ingredients as is and as various dilutions in aqua and ethanol. A positive SPT reaction was defined as a wheal with a mean diameter of at least 3 mm and equal to or greater than half of the diameter of the histamine wheal.

Serum total IgE was measured using the Phadia UniCAP System (Phadia, Uppsala, Sweden). A total IgE level less than 110 kU/L was regarded as normal.

### Open Skin Testing

An open skin test (ie, an open application test) was performed to confirm the diagnosis of contact urticaria due to oxidative hair dye. We tested the hair dye products both as is and with the oxidant (ie, hydrogen peroxide). The test substance was applied thinly on a 5 × 5-cm area of healthy skin on the forearm. The test area was inspected at 20 minutes, and if the result was negative, the

application was repeated in the same area for another 20 minutes. The test area was then reinspected and the test material removed. All the open skin test results were read and interpreted by a dermatologist. A positive open skin test reaction was defined as one or several urticarial wheals appearing on the test area.

### Patch Testing

Only the patients with a history of eczema underwent patch testing, for which we used the Finn Chamber method (Epitest, Tuusula, Finland) according to the recommendations of the International Contact Dermatitis Research Group. The tests were read 2 or 3 times, depending on the day of the week on which the test patches were applied. PPD and TDS were patch tested as 1% in petrolatum with commercially available test substances (Trolab; Almirall Hermal GmbH, Reinbek, Germany).

### Lung Function Tests and Fractional Exhaled Nitric Oxide

We performed the flow-volume spirometry and bronchodilation tests in accordance with the American Thoracic Society criteria,<sup>38</sup> using a standard spirometer (Spirostar USB; Medikro, Kuopio, Finland) and the predicted values for the Finnish population. We performed the bronchial challenge with histamine according to the method described previously.<sup>39</sup> We measured the provocative dose causing a 15% reduction in forced expiratory volume in 1 second (FEV<sub>1</sub>) (PD<sub>15</sub>). Bronchial hyperresponsiveness was graded as follows: severe, PD<sub>15</sub> less than 0.1 mg; moderate, PD<sub>15</sub> of 0.1 to 0.4 mg; mild, PD<sub>15</sub> of 0.4 to 1.6 mg; and no hyperresponsiveness, PD<sub>15</sub> greater than 1.6 mg. Serial peak expiratory flow measurements during days at work and days off were performed according to the method of Burge.<sup>40</sup> We measured exhaled nitric oxide using an online chemiluminescence analyzer (NIOX; Aerocrine AB, Solna, Sweden) and interpreted it according to current recommendations.<sup>41,42</sup>

### Specific Inhalation Challenge Tests

Patients with suspected OA or OR underwent SICs in a 6-m<sup>3</sup> challenge chamber for 2 or 3 subsequent days, each with a 24-hour follow-up. In the control tests, lactose powder was puffed into the breathing zone from a bowl with pressured air in 1-minute intervals for 30 minutes. The SIC with oxidative hair dye was performed as a work simulation: the patient mixed a dose (60–80 mL) of oxidative hair dye with an oxidant that contained hydrogen peroxide (3%–12%) for 30 minutes. The hair dye product suspected to have caused the patient's respiratory symptoms was used. Six patients also underwent an SIC with a hair bleach product that contained persulfates and an oxidant that contained hydrogen peroxide.

The test result was considered positive for OA when there was a sustained decrease in FEV<sub>1</sub> of 20% or more from the prechallenge value, in the absence of significant (≥10%) changes in the control test.<sup>43</sup> The positive bronchial reactions were classified into 3 patterns: early reactions occurred within an hour after the end of exposure, late reactions within 1 to 8 hours, and dual reactions consisted of both early and late reactions.

The degree of rhinorrhea and nasal blockage of patients with suspected OR was evaluated by anterior rhinoscopy before the SIC and approximately 20 minutes after the end of the SIC. Rhinorrhea and nasal blockage were scored on a range of 0 (dry or thin mucosa) to 3 points (dripping mucus or swelling of the mucosa). We also measured the amount of nasal secretion running out of the patient's nose and to the vestibulum of the nostrils. The results were interpreted according to the scoring system described by Hytonen et al.,<sup>44</sup> and OR was considered to be the case if the control SIC test result was negative and the score changed by 4 points or more in both nostrils in the SIC with a hair dye. Nasal secretion of

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